ORIGINAL RESEARCH

Protein Intake and Long-term Change in Glomerular Filtration Rate in the Jackson Heart Study

Rakesh Malhotra, MD, MPH,[*] Loren Lipworth, ScD,[†,‡,§] Kerri L. Cavanaugh, MD, MHS,[†,¶] Bessie A. Young, MD,[**] Katherine L. Tucker, PhD,[††] Teresa C. Carithers, PhD,[‡‡] Herman A. Taylor, MD, MPH,[§§] Adolfo Correa, MD, PhD,[¶¶] Edmond K. Kabagambe, DVM, MS, PhD,[†,‡,§] and T. Alp Ikizler, MD[†,¶]

Objective: Dietary protein intake could have deleterious renal effects in populations at risk for chronic kidney disease. Here, we examined whether higher protein intake (≥80th percentile of energy from protein) is associated with decline in kidney function and whether this decline varies by diabetes status.

Design: Observational cohort study.

Subjects and Settings: Participants were African-Americans (n = 5,301), who enrolled in the Jackson Heart Study between 2000 and 2004.

Methods: Dietary intake was assessed using a validated food-frequency questionnaire at baseline, and serum creatinine was measured at baseline (visit 1) and 8 years later (visit 3). Estimated glomerular filtration rates (eGFRs) at baseline and follow-up were computed using the chronic kidney disease epidemiology collaboration equation.

Main Outcome Measure: The change in eGFR was computed by subtracting eGFR at visit 1 from that at visit 3.

Results: Of 3,165 participants with complete data, 64% were women, 57% had hypertension, and 19% had diabetes. The median (25th, 75th percentile) percent energy intake from protein was 14.3 (12.4, 16.4), comparable to that reported for the general US population (15% of energy). During a median (25th, 75th percentile) follow-up of 8.0 (7.4, 8.3) years, eGFR declined by 10.5% from a mean (SD) of 97.4 (17.5) to 86.9 (21.3) mL/min/1.73 m^2. In the fully adjusted model, consumption of protein as percent of energy intake in lowest and highest quintiles was associated with decline in eGFR among diabetic subjects. The analysis of variance with a robust variance estimator was used to determine whether long-term change in eGFR significantly varies by protein intake.

Conclusions: Our results show that, among African-Americans with diabetes, higher protein intake as a percent of total energy intake is positively associated with greater decline in eGFR in analyses that accounted for risk factors for kidney disease.

[*]*Division of Nephrology and Hypertension, Department of Medicine, University of California San Diego, San Diego, California.*

[†]*Vanderbilt Center for Kidney Disease, Nashville, Tennessee.*

[‡]*Division of Epidemiology, Department of Medicine, Vanderbilt University Medical Center, Nashville, Tennessee.*

[§]*Jackson Heart Study Vanguard Center at Vanderbilt University Medical Center, Nashville, Tennessee.*

[¶]*Division of Nephrology and Hypertension, Department of Medicine, Vanderbilt University Medical Center, Nashville, Tennessee.*

[**]*Division of Nephrology, Department of Medicine, VA Puget Sound Health Care System, Kidney Research Institute, University of Washington, Seattle, Washington.*

[††]*Biomedical and Nutritional Sciences, Center for Population Health, University of Massachusetts Lowell, Lowell, Massachusetts.*

[‡‡]*School of Applied Sciences, Nutrition and Hospitality Management, University of Mississippi, Jackson, Mississippi.*

[§§]*Cardiovascular Research Institute, Morehouse School of Medicine, Atlanta, Georgia.*

[¶¶]*Department of Medicine, Jackson Heart Study, University of Mississippi Medical Center, Jackson, Mississippi.*

E.K.K. and T.A.I. contributed equally as senior authors.

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Address correspondence to Rakesh Malhotra, MD, MPH, Division of Nephrology-Hypertension, University of California San Diego, 3350 La Jolla Village Drive, Mail Code 9111-H, San Diego, CA 92161. E-mail: r3malhotra@ucsd.edu

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Introduction

CHRONIC KIDNEY DISEASE (CKD) is a major public health problem, with estimated prevalence of 14%-16% of the adult population in the United States.[1,2] Individuals with CKD often progress to end-stage renal disease (ESRD), a condition that requires costly dialysis or transplantation and is associated with substantial morbidity and mortality.[3] Although diabetes and hypertension are major contributors to kidney disease,[4,5] other modifiable risk factors, including diet, may contribute to the development of incident CKD and further decline of kidney function.[6,7]

In experimental animal models, high-protein diet is known to increase glomerular pressure and hyperfiltration and, thus, results in glomerular hypertrophy and sclerosis.[8,9] High-protein diet, especially its metabolite byproducts, may also lead to alteration of homeostasis of vasoactive compounds and direct injury of podocyte and kidney cells.[10,11] These primary hypotheses have generated considerable interest and guided investigation in humans to determine the role of dietary protein intake in the pathogenesis of CKD.

Previous studies,[12-14] albeit small in sample size, demonstrated that high protein intake was associated with a modest decline in kidney function. Among 489 women with reduced renal function at baseline (estimated glomerular filtration rate [eGFR] <80 mL/min/1.73 m^2) in the Nurses' Health Study, higher consumption of nondairy animal protein was associated with a decline in eGFR (-1.21 mL/min per 1.73 m^2 per 10 g increase in protein intake) over a 11-year span.[15] On the opposite extreme, the landmark Modification of Diet in Renal Disease (MDRD) trial that enrolled CKD patients without diabetes showed no benefit from lowering protein intake.[16] Although both the Nurses' Health Study and the MDRD study were primarily conducted among affluent white populations, the 2 studies varied with regard to study design, length of follow-up, and inclusion of subjects with polycystic kidney disease, attributes that could explain the null results in the MDRD study. We previously published a nested case-control study within the Southern Community Cohort Study (SCCS) showing that higher percentage protein intake was associated with increased risk of incident ESRD, especially among black individuals with diabetes.[17] However, the SCCS and several of the previous large studies lacked repeated measures on eGFR or a large number of minority participants with diabetes, who might have greater susceptibility for decline in kidney function. There are also limited longitudinal data of the association of high protein intake and decline in eGFR in African-Americans (AA). To that end, we hypothesized that higher protein intake would be associated with decline in kidney function and that patients with diabetes would experience greater declines in eGFR over an 8-year follow-up period. To test this hypothesis, we evaluated decline in eGFR among AA participants of the Jackson Heart Study (JHS).

Materials and Methods

Study Participants

Participants in the present study are from the JHS, which enrolled noninstitutionalized AA participants (n = 5,301) from 3 separate counties (Hinds, Madison, or Rankin) in Jackson, Mississippi between 2000 and 2004. The Institutional Review Boards at the University of Mississippi Medical Center, Jackson State University and Tougaloo College approved the JHS study. All participants provided written informed consent.

For this analysis, we excluded participants who did not have dietary data (n = 164), missing serum creatinine (sCR) measurements at baseline or follow-up (n = 1,521) and had implausible energy intakes (less than or equal to 600 kilocalories per day or above 6,000 kilocalories daily) or missing >5 items on the food-frequency questionnaire (FFQ) (n = 230). We further excluded 34 participants who were missing data on alcohol intake, smoking, body mass index, or diabetes status, 33 participants with history of dialysis at baseline and 154 participants with baseline eGFR <60 mL/min/1.73 m^2, leaving 3,165 participants for the final analyses (Fig. 1).

Protein Intake

Protein intake was estimated from a validated FFQ administered at visit 1.[18] Correlation coefficients between protein intake estimated from the FFQ and four 24-hour dietary recalls among 498 participants were 0.45 among men and 0.50 among women, which are comparable to those from other studies.[19,20]

Change in Estimated Glomerular Filtration Rate

The change in eGFR was computed by subtracting eGFR at follow-up (visit 3) from eGFR at baseline (visit 1). Both eGFR values were computed using the chronic kidney disease epidemiology collaboration equation.[21] As sCR was not measured at visit 2, eGFR measurements were not available for this time point. sCR was measured with a multipoint enzymatic spectrophotometric assay (Vitros CREA dry reaction slides on a Vitros 950 Ortho-Clinical Diagnostics analyzer, Raritan, NJ) and optimally calibrated to measurements traceable to isotope dilution mass spec using a Deming regression model at baseline (visit 1) and at follow-up (visit 3). All measurements were made centrally at the University of Mississippi Medical Center Laboratory Reading Center where measurements were completed *en bloc* such that each participant had their visit 1 and visit 3 sCR concentrations determined at the same time to minimize analytic drift.[21]